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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,492	03/24/2006	Michal Eisenbach-Schwartz	EIS-SCHWARTZ26A	1098

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,492	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 30-43* is/are pending in the application.

4a) Of the above claim(s) *3,5,11,12 and 30-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-10,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/7/05;7/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. The amendment of 28 July 2008 in the claims has been entered in full. Claim 4 is amended. Claims 11 and 30-43 are withdrawn by Applicant as drawn to non-elected invention.

Election with traverse

2. Applicant's election with traverse of Group I, claims 1-14, in the reply filed on 28 July 2008 is acknowledged.

3. The traversal is on the ground(s) that the Examiner (i) has not explained that the two alleged inventions do not share a special technical feature, especially since the common special technical feature is the eye-drop vaccine; (ii) has no authority to require restriction between a product and a process of use of said product, based upon the regulation referring to lack of unity under 37 CFR 1.475, 37 CFR 1.475(b) (2). Applicant further asserts that since the methods of three independent claims are considered to be drawn to the same method of use invention of Group II by the Examiner, the "applicable regulations preclude the present election requirement". Applicant thus requests the withdrawal of the restriction requirement. Applicant's arguments are fully considered, however, are not found to be persuasive. Examiner acknowledges that no specific reason was stated for the lack of unity between Groups I and II. However, the inventions

listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: This PCT rule defines special technical features as technical features that identify a contribution which each of the claimed inventions, considered as a whole, makes over prior art (See M.P.E.P. 1850). Claim 1 is anticipated by prior art. Eisenbach-Schwartz et al., (US 2002/0037848 A1, 3/28/02, filed 1/22/01) teach pharmaceutical compositions comprising Copolymer 1 or Cop 1 as an active principle, for the use as a vaccine to raise T cells activated thereagainst in vivo (page 11, para 0105) by systemic or local administration such as intraocular (page 11, para 0108). Therefore, claim 1 of Group I lacks a special technical feature and cannot share one with the process claims of Group II. Thus, the apparent "special technical features" of claims 1-14 (Group I), cannot form the basis of unity of invention. Groups I-II do not possess special technical features as set forth above. Furthermore, the claims in the national stage application can be restricted on the basis of lack of unity of invention at the discretion of the examiner. See 37 CFR 1.499.

4. Additionally, Applicant reminds of the election requirement in the Office Action dated 28 May 2008 from among the 32 sequences of Table 1, page 12 of specification. However, pursuant to the 13 June 2008 telephonic interview between Supervisory Patent Examiner Jeffrey Stucker and Attorney Roger Browdy, the Interview Summary dated 25 June 2008 indicated that Examiner

Stucker agreed that the portion directed to the requirement for specific sequences (top of page 3 of the action) will be withdrawn in consideration of Mr. Browdy's arguments that there are no specific sequences claimed. Based on this agreement, Applicant considered the election of a specific sequence from among groups A-AF as not necessary to be responsive for this restriction requirement. Applicant's arguments are considered and found to be persuasive. As agreed upon during the interview and summarized in the ensuing Office Action dated 25 June 2008, the restriction requirement for a specific sequence from among Groups A-AF is withdrawn.

5. Finally, as stated in the previous Office Action, it is reiterated that upon allowance of an elected product, the first enabled method of using the claimed product will be rejoined to the examined Invention. However, until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims should be maintained (*In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b), 1184 O.G. 86 March 26, 1996).

The requirement is still deemed proper and is therefore made FINAL.

6. Claims 3, 5, 11-12, and 30-43 are withdrawn, as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 28 July 2008.

7. Claims 1-2, 4, 6-10, and 13-14, drawn to an eye-drop vaccine for therapeutic immunization of a mammal, are being considered for examination in the instant application.

8. Applicant's election of the following species without traverse in the reply filed on 28 July 2008 is acknowledged: Copolymer 1 as the active agent; disease, disorder or condition as the cause of neuronal degeneration; preventing or inhibiting neuronal secondary degeneration as the action of eye-drop vaccine; and glaucoma as the disorder or condition.

Oath/Declaration

9. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.
It was not executed in accordance with either 37 CFR 1.66 or 1.68. The dates of the priority applications on page 1 of the declaration are not matching with that on the application data sheet. For example, PCT/IL04/000006 has 6/1/04 and application number 60/438,310 has 7/1/03.
Appropriate correction is required.

Claim Objections

10. Claims 1, 2 and 4 are objected to because of the following informalities:

Claims 1, 2 and 4 recite non-elected species.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 – Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-2, 4, 6-10 and 13-14, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Cop 1 eye-drop vaccine for reducing the death of retinal ganglion cells following the rise in intraocular pressure (IOP) in glaucoma in a rat intraocular pressure model, does not reasonably provide enablement for the eye-drop vaccine for preventing or inhibiting neuronal secondary degeneration due to any disease, disorder or condition in the CNS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

12. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, include the nature of

the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

13. The claims recite an eye drop vaccine comprising Cop-1 as the active agent, without or with a soluble adjuvant such as cytokine (e.g. IL-1, IL-12, IFN-γ or GM-CSF) for therapeutic immunization for preventing or inhibiting neuronal secondary degeneration in the CNS, wherein the disease, disorder or condition is glaucoma (claims 1-2, 4, 6-10).The claims further recite the periodic administration of the eye drop vaccine to a non-multiple sclerosis patient or a glaucoma patient (claims 13, 14). As noted above, claim 2 has both elected and non-elected subject matter. Based upon Applicant's election of species without traverse, for purposes of consideration and current examination on the merits, claim 2 is interpreted as directed to an eye-drop vaccine for preventing or inhibiting neuronal secondary degeneration due to a disease, disorder or condition in the CNS.

14. The instant specification teaches that copolymer 1 or Cop 1 or glatiramer acetate is a non-pathogenic synthetic random copolymer composed of 4 amino acids L-Glu, L-Lys, L-Ala and L-Tyr, that cross-reacts functionally with myelin basic protein (MBP) (page 5, lines 4-10; page 8, line 6), and with a wide variety of self-reactive T cells (page 4-5, line 1). The specification also teaches that Cop

1 is an approved drug for multiple sclerosis and that it is mostly administered subcutaneously (s.c.). The specification further teaches that neurodegenerative diseases are associated with ongoing neuronal loss, the primary risk factors leading to additional or secondary neuronal degeneration mediated by self-compounds like glutamate, nitric oxide or reactive oxygen species (page 2, lines 3-6). Additionally, T cells reactive to MBP demonstrated neuronal protection in rat models of partially crushed optic nerve and of spinal cord injury. Still further, the specification discloses that glaucoma is a slow-progressing optic neuropathy which may or may not result from increased IOP (page 2, lines 12-23). The specification teaches that Cop 1 vaccination without adjuvant in a chronic or acute IOP rat model (s.c. or eye-drop) reduces IOP induced loss of retinal ganglion cells (RGC) (Example 4, Figure 4A, B; Example 5), wherein the effect is immune or T cell mediated as thymectomized rats do not demonstrate the vaccine effect (Figure 3A; Example 3). However, the instant specification does not provide sufficient guidance and information with regards to the eye-drop Cop 1 vaccine for preventing or treating any secondary neuronal degeneration arising in the CNS that might follow any disease, disorder or condition. The specification does not enable the claimed eye-drop vaccine for the prevention or inhibition of any complex neuronal degeneration arising due to the even more complex neurodegenerative disorders, wherein the primary factors are yet to be uncovered. The specification also does not enable the claimed eye-drop vaccine for preventing or inhibiting the loss or RGC in glaucoma arising due to other

factors like genetic reasons, etc. Since preventing indicates stopping of the pathogenesis, and since the instant teachings cannot be reasonably extrapolated to preventing or inhibiting of neuronal degeneration, undue experimentation would be required of a skilled artisan to make and use the claimed product.

15. Relevant art teaches that Cop 1 can be substituted for natural myelin antigen in the rat ocular hypertension model, wherein Cop 1 can reduce significantly the RGC loss without affecting the IOP (Schori et al., PNAS 98: 3398-3403, 2001; Abstract), when administered intraperitoneally. The reference further teaches that glaucoma, the leading cause of blindness is a chronic condition of optic nerve, usually, though not always associated with elevated IOP (concluding para). Whitson teaches that although elevated IOP is a risk factor for glaucoma, several other factors are involved, e.g. old age, ethnicity, genetic factors, vascular disease, etc. Normal tension glaucoma accounts for about 30% of glaucoma (Exp Opin Pharmacother. 8: 3237-3249, 2007; Introduction). However, the relevant art or the specification fail to provide the guidance for the use of an eye-drop Cop-1 vaccine having the function of preventing or inhibiting secondary neuronal degeneration due to any primary disease, disorder or condition, or even glaucoma caused by other factors aside from elevated IOP.

16. Furthermore, it is uncertain that the dosage and frequency of the Cop 1 vaccine administered in the eye-drop route will achieve the required immunization for the claimed function of the vaccine. The specification assumes that about 10% of eye drops enter the circulation. Different disorders would

require different amounts of eye drop administration to achieve an effective dosage in the circulation. Given the sole example of the eye-drop vaccine having the function of reducing RGC death in the rat intraocular pressure model, it is unpredictable as to whether the eye-drop vaccine will get into the blood system in adequate amounts and successfully activate T cells sufficient to induce an immune response for preventing or inhibiting secondary neuronal degeneration caused by any disorder in the CNS, which might require different dosages of the eye-drop vaccine, administered at different intervals. Based upon the lack or adequate information in the specification and in the relevant art, and knowing that the eye-drop vaccination is not a routine mode of immunization for any CNS disorder, aside from optic nerve related disorder or glaucoma, undue experimentation would be required of the skilled artisan to determine the optimal dosage, number of booster administrations, and periodic interval of eye-drop administration to achieve the claimed function of the eye-drop vaccine with predictability and a reasonable amount of success.

17. Due to the large quantity of experimentation necessary for an eye-drop vaccine having the functional limitations of preventing and inhibiting secondary neuronal degeneration resulting from any CNS condition; the lack of sufficient direction/guidance presented in the specification regarding the same; the complex nature of the invention; the state of the art which has yet to determine an eye-drop vaccine; undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 1, 6-8 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Eisenbach-Schwartz et al., (US 2002/0037848 A1, 3/28/02, filed 1/22/01, with a prior filing date of 20 July 2000, US application number 09/620216). The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another", or by an appropriate showing under 37 CFR 1.131.

19. The claims recite an eye drop vaccine comprising Cop-1 as the active agent, without or with a soluble adjuvant such as cytokine for therapeutic immunization (claims 1, 6-8, 10).

20. Eisenbach-Schwartz et al., teach pharmaceutical compositions comprising Copolymer 1 or Cop 1 as an active principle, for the use as a vaccine to raise T cells activated thereagainst in vivo (page 11, para 0105) by systemic or local administration such as intraocular (page 11, para 0108). The art further teaches that Cop 1 can be administered with an adjuvant for immunization, which can include cytokines (pages 10-12, para 0101, 0116). Furthermore, the publication teaches the use of Cop 1 in the absence of adjuvants for immunization (page 19, para 0184). Although the reference does not teach an eye-drop vaccine, this limitation present in the preamble merely provides an intended use, which does not add patentability to the claimed vaccine composition. As stated in MPEP ("where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation") *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997). As the reference teachings meet the claimed limitations of the Cop 1 vaccine, the reference anticipates the invention.

21. Claims 1, 6-8 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Eisenbach-Schwartz et al., (US 2002/0037848 A1, 3/28/02).

22. For reasons explained above, the reference teachings meet the claimed limitations, thus the reference anticipates the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. Claims 1, 8 and 9 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Eisenbach-Schwartz et al., (US 2002/0037848 A1, 3/28/02) in view of Scott et al. (US Patent No. 5,571,515, issued on 5 November 1996).

25. The claims recite an eye drop vaccine comprising Cop-1 as the active agent, with a soluble adjuvant such as cytokine (e.g. IL-1, IL-12, IFN-γ or GM-CSF) for therapeutic immunization.

26. The teachings of Eisenbach-Schwartz et al. are set forth above.

27. Eisenbach-Schwartz et al. do not teach the administration of adjuvants comprising cytokines, e.g. IL-1, IL-12, IFN-γ or GM-CSF.

28. Scott et al teach pharmaceutical compositions comprising a vaccine comprising an antigen and an effective adjuvanting amount of interleukin-12 or IL-12 (col 2, lines 30-36).

29. Iit would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the eye-drop vaccine comprising the active agent as Cop 1 as taught by Eisenbach-Schwartz et al. by adding a soluble adjuvant consisting a cytokine such as IL-12 to the vaccine as taught by Scott et al. The person of ordinary skill would have been motivated to use the vaccine with IL-12, because IL-12 can increase the host cell's mediated immune response for effective protection against an infection by a pathogen (Scott et al., col 1, lines 14-18). The person of ordinary skill in the art would have expected success because experiments to immunize with vaccines comprising adjuvants as cytokines, were already known in the art at the time the invention was made.

30. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

31. No claims are allowed.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

34. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD

23 October 2008

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649